REMARKS

The claims have been amended. Support for the amendments is found, for example, on page 6, lines 6-11; page 7, lines 7; page 8, lines 18-29; and example 1 at pages 13 and 14. No new matter has been added.

Rejections Under 35 U.S.C. §102(b)

The Examiner rejected claims 1-5 and 13 as anticipated by Mills et al. According to the Examiner, Mills et al. describe the production of PCR products that include both normal dNTPs and derivatives thereof, including inosinic acid labeled nucleotides. The Examiner argues that the PCR products disclosed by Mills et al. meet the structural requirements of previous claims 1-5 and 13.

Claim 1 has been amended to recite a hybridization probe "consisting of a first region that is complementary to a target nucleotide sequence" and "a second region having a sequence that comprises one or more nucleotides or nucleotide derivatives selected from the group consisting of labeled nucleotides, labeled nucleotide derivatives, unlabeled nucleotides and unlabeled nucleotide derivatives" The second region has a sequence that: "a) comprises at least one nucleotide or nucleotide derivative having weaker affinity of hydrogen bonding in base pairing with bases of the target nucleotide sequence when compared with that of hydrogen bonding in an a/t pair, in an a/u pair, or in a g/c pair a; b) comprises either or both of at least one labeled nucleotide and labeled nucleotide derivatives; and c) is incapable of hybridizing under stringent conditions to any nucleotide sequence of the target nucleotide sequence."

Claim 13 has been amended to recited a hybridization probe "comprising a first region having a sequence which is identical to a complementary nucleotide sequence of a target nucleotide sequence" and "a second region having a sequence comprising one or more nucleotides or nucleotide derivatives selected from the group consisting of labeled nucleotides, labeled nucleotide derivatives, and unlabeled nucleotide derivatives". The second region has a sequence that: "a) comprises at least one nucleotide or nucleotide derivative having weaker affinity of hydrogen bonding in base pairing with bases of the target nucleotide sequence when compared with that of hydrogen bonding in an a/t pair, in an a/u pair, ~~and~~ or in a g/c pair; b) comprises either or both of at least one labeled nucleotide and labeled nucleotide derivatives; and

c) is incapable of hybridizing under stringent conditions to any nucleotide sequence of the target nucleotide sequence."

The nucleic acid molecules formed by the methods described in Mills et al. are generated using RNA polymerase. In Mills et al., inosine is substituted for guanosine in order to reduce secondary structures that can arise from self-hybridization. Of course, inosine does base-pair with cytosine, albeit more weakly than does guanosine. Thus, the entire nucleic acid molecule created by the method of Mills et al., both the primer portion and the RNA polymerase produced portion, base-pairs with and hybridizes to the template molecule along the entire length of the template molecule. Thus, it can be assumed that the molecules created by the method of Mills et al., including the portion of the molecules that includes inosine, hybridizes under stringent conditions to the template molecule. In contrast, the hybridization probes of the presently claimed invention include a region ("the second region") that "is incapable of hybridizing under stringent conditions to any nucleotide sequence of the target nucleotide sequence". Using the method of Mills et al., which relies on RNA polymerase, it is not possible to synthesize nucleic acid molecules having two completely different structural characteristics. That is, it is impossible to synthesize nucleic acid molecules that include both a first region having a sequence which is complementary to a target nucleotide sequence and a second region having a sequence comprising one or more labeled nucleotides or labeled nucleotide derivatives, wherein the second region has a sequence which is incapable of hybridizing under stringent conditions to any nucleotide sequence of the target nucleotide sequence. Accordingly, Mills et al. cannot anticipate any of present claims 1-5 and 13, and Applicants respectfully request that the rejection of these claims under 35 U.S.C. §102(b) be withdrawn.

Rejections Under 35 U.S.C. §103

The Examiner rejected claims 11 and 14 under 35 U.S.C. §103 as obvious in view of Mills et al. and Chenchik et al. According to the Examiner, Chenchik et al. discloses kits that "comprise reagents used in performing PCR" which kits "may also comprise added reagents, including terminal transferase". According to the Examiner, it would have been obvious to include the inosine used in the PCR method of Mills et al. in the kits of Chenchik et al.

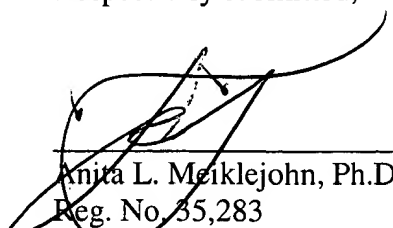
In order to make a *prima facie* case of obviousness there must be a motivation to combine the teachings of the cited references. "The showing of the motivation to combine must be clear

and particular, it must be supported by actual evidence." *In re Dembiczak*, 175 F.3d 994, 999 (Fed. Cir. 1999). In the present case the Examiner has not provided any motivation to combine the cited references, much less a "clear and particular" motivation. In fact, no motivation exists. Chenchik et al. describes a method for suppressing the amplification of unwanted DNA fragments during PCR. The method involves attaching adapters to the ends of DNA fragments. These adapters can be attached using, for example, terminal transferase (column 7, lines 18-27). Due to the presence of the self-complementary adapter, certain DNA molecules become self-annealing. Thus, these molecules form a secondary structure that interferes with PCR amplification. Thus, Chenchik et al. uses terminal transferase to create nucleic acid molecules that will readily form a secondary structures. The purpose of Mills et al. is, of course, the exact opposite. Mills et al. includes inosine in the disclosed PCR amplification to create nucleic acid molecules that will not readily form a secondary structure. Because Chenchik et al. describes the inclusion of terminal transferase in a PCR kit for reasons that are directly at odds with Mills et al.'s rationale for including inosine in a PCR reaction, there can be no motivation modify the kit described by Chenchik et al. by adding the inosine used by Mills et al. For this reason it is Applicants' position that the Examiner has not made a prima facie case that claims 11 and 14 are obvious in view of Chenchik et al. taken with Mills et al. In view of the forgoing, Applicants respectfully request that the rejection of claims 11 and 14 under 35 U.S.C. §103 be withdrawn.

Enclosed is a $950.00 check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: 8 Sept 2004



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